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EXAMINER

WOODWARD, M

ART UNIT

PAPER NUMBER

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1813

DATE MAILED:

04/24/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 10/25/95 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), — days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

- | | |
|---|---|
| 1. <input checked="" type="checkbox"/> Notice of References Cited by Examiner, PTO-892. | 2. <input type="checkbox"/> Notice of Draftsman's Patent Drawing Review, PTO-948. |
| 3. <input checked="" type="checkbox"/> Notice of Art Cited by Applicant, PTO-1449. | 4. <input type="checkbox"/> Notice of Informal Patent Application, PTO-152. |
| 5. <input type="checkbox"/> Information on How to Effect Drawing Changes, PTO-1474. | 6. <input type="checkbox"/> |

Part II SUMMARY OF ACTION1. ☒ Claims 60-72, 74-89 are pending in the application.Of the above, claims — are withdrawn from consideration.2. ☒ Claims 1-59, 73 have been cancelled.3. ☐ Claims — are allowed.4. ☒ Claims 60-70, 72, 74-89 are rejected.5. ☒ Claims 73 are objected to.6. ☐ Claims — are subject to restriction or election requirement.7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.8. ☐ Formal drawings are required in response to this Office action.9. ☐ The corrected or substitute drawings have been received on —. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on —, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).11. ☐ The proposed drawing correction, filed —, has been ☐ approved; ☐ disapproved (see explanation).12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. —; filed on —.13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.14. ☐ Other**EXAMINER'S ACTION**

In view of the papers filed October 25, 1995 (Cert. Mail. October 16, 1995(Paper No. 1¹2)) and Paper No. 4 (March 27, 1995), it has been found that this application, as filed, through error and without any deceptive intent, improperly set forth the inventorship, and accordingly, this application has been
5 corrected in compliance with 37 C.F.R. § 1.48. The inventorship of this application has been changed by the deletion of Kathelyn Steimer, Ray S. Pescador, Carlos George-Nascimento, Deborah Parkes, Rob Hallewell, Philip J. Barr and Martha Truett as co-inventors.

10 Applicant's arguments filed October 25, 1996 (Cert.Mail. October 16, 1995) and March 11, 1996 (Cert.Mail. March 6, 1996) have been fully considered but they are not deemed to be completely persuasive.

15 The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

In the Information Disclosure Statement filed October 16, 1995 applicant cites SN 907185 and SN 071674 neither of which appears to be assigned to applicant. Applicant is requested to clarify the record concerning the status of
20 these applications as prior art with regard to the instantly claimed invention. The examiner concludes from the citation of the '185 and '674 applications that applicant had their respective teachings available to him prior to invention of the instantly claimed subject matter.

25 The rejection of claims 60-80 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the

subject matter which applicant regards as the invention is withdrawn in view of the amendments to the claims.

The rejection of claims 60, 61 and 63-72 under 35 U.S.C. § 102(b) as being clearly anticipated by Foecking et al. (1986) is withdrawn as applicant is correct that the Foecking et al. vector does not contain the SV40 origin of replication. However, applicant's remarks concerning the difference in the HCMV sequences present in the instantly claimed inventions and that of Foecking et al. are not on point because the instant claims, with the exception of claim 71, are not limited to the inclusion of only those sequence elements recited by applicant.

The rejection of claim 62 under 35 U.S.C. § 103 as being unpatentable over Foecking et al. (1986) is withdrawn for the reasons above.

The rejection of claims 74 and 75 under 35 U.S.C. § 103 as being unpatentable over the combined teachings of Foecking et al. (1986) and van Zonneveld et al. (1986) is withdrawn for the reasons above.

Claims 65, 82-89 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 65 and 82 are vague and indefinite as they do not clearly establish that the intron proximate to the 3' end of the HCMV IE1 promoter is to be the first intron of the HCMV IE1 region.

The relationship between claims 60, 81 and 87 is puzzling as it is unclear why one would put in an additional origin of replication and polyadenylation site into the vector of claim 60.

Claims 60-70 and 72-89 are rejected under 35 U.S.C. § 112, first

paragraph, as the specification, as originally filed, does not provide support for the invention as is now claimed.

The specification as originally filed contains example 2.3.2 which sets forth a definition of "a transcription regulatory region from human
5 cytomagalovirus." From the description in the specification one of skill in the art would recognize the "transcription regulatory region" as being the 1.7 kbp SspI-SalI set forth in the specification. However, given claims 63 and 65 it is clear that applicant now intends that "transcription regulatory region" has a different meaning. It is clear from claims 63 and 65 that the scope of
10 "transcription regulatory region" as now envisioned is not that of the original specification because both the "enhanced promoter" of claim 63 and "the first intron" of claim 65 are no longer required elements. In truth, it is not at all clear what is a required element in view of claim 63. The words of the CAFC in *Genentech Inc. v. The Wellcome Foundation Ltd.* (35 USPQ2d 1161, Fed.Cir.
15 1994) at page 1167 appear to be appropos:

These diverse definitions reflect either inartful drafting, a conscious attempt to create ambiguity about the scope of the claims, or a desire to claim a wide variety of materials not described or enabled in the specification.

20 It is noted that applicant's traversal of this rejection at pages 11-12 of Paper No. 10 does not address the issue of written description.

Claims 79 and 80 are again rejected under 35 U.S.C. § 112, first paragraph, as the specification fails to adequately teach how to make and/or use
25 the invention, i.e. failing to provide an enabling disclosure.

Applicant argues that the specification at pages 57 and 58 and Figure 29 offer direction as to how to make the intron of claims 79 and 80. This is

simply not the case as what is set forth at pages 57 and 58 and Figure 29 is guidance on the preparation of an expression vector which contains a fragment of the HCMV genome which fragment also contains the intron. There is nothing to indicate how to prepare the intron. Applicant further argues that the increase in expression by constructs containing transcriptional elements in addition to the intron is guidance as to how to use the intron per se. The examiner does not find that an example of such limited scope provides guidance as to how to use the intron alone or in combination with other regulatory elements in as much as there is no clear evidence concerning the function/activity of the intron per se.

Claims 79 and 80 are again rejected under 35 U.S.C. § 112, first paragraph, as the specification, as originally filed, does not provide support for the invention as is now claimed.

Applicant is incorrect that claims 79 and 80 are originally filed claims. Applicant is encouraged to review SN 07/138894 which as originally filed presented 59 claims.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as the specification, as originally filed, does not provide support for the invention as is now claimed.

The specification as originally filed is silent with regard to "a transcription regulatory region homologous to a region present in human cytomegalovirus." Similarly the specification is silent with regard to "homologous to the first HCMV IE1 intron," "homologous to a SV40 polyadenylation sequence,"
5 "homologous to a SV40 origin of replication" and "homologous to a sequence present in the first intron proximal." The specification is silent as to the meaning of homologous much less what elements of the recited polynucleotides are relevant to its function. Absent such disclosure one of skill might obtain a homologous sequence devoid of function. In as much as one cannot discern
10 which homologous sequences are nonfunctional prior to construction of the expression systems one is invited to experiment to find those embodiments which are operable. Such unguided experimentation is one of the hallmarks of undue experimentation.

Claims 60-70 and 74-89 are rejected under 35 U.S.C. § 112, first
15 paragraph, for the reasons set forth in the objection to the specification.

At page 20 applicant states:

Applicants have considered the additional prior art made of record
20 (and not relied upon) by the present Office Action (Paper No. 8, pages 8-10), and acknowledge the Office's position that the subject art does not affect the patentability of the present invention.

**Unfortunately, the Office did not take and does not now take the position that the subject art does not affect the patentability of the present invention. The additional art was supplied in anticipation that applicant
25 would amend his claims so as to overcome the art relied upon in the recited grounds of rejection and the prior art as a whole.**

The following is a quotation of the appropriate paragraphs of 35 U.S.C.

§ 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 60, 61, 63-70, 76, 77, 78 and 81-89 are rejected under 35 U.S.C. § 102(e) as being clearly anticipated by Gorman (US 5,024,939).

At column 17 Gorman (US 5,024,939) describes the construction of an expression plasmid comprising the CMV enhancer, promoter and splice donor site, an Ig variable region intron and splice acceptor sequence, and the polyadenylation site and transcription termination site of the early region of SV40. At column 13 vectors containing an SV40 origin of replication are described and the role which it plays in replication in mammalian cells set forth.

Claims 79 and 80 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Boshart et al. (1985).

Claims 79 and 80 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Stenberg et al. (1984).

Claims 60-70, 72 and 74-89 are again rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Chapman et al. (1991).

Applicant has yet to provide evidence that the broadly claimed invention of claims 60-70, 72 and 74-89 has written description in the application as originally filed.

Claim 62 is rejected under 35 U.S.C. § 103 as being unpatentable over Gorman (US 5,024,939).

The vectors taught by Gorman do not appear to contain the SalI site recited in claim 62. It is well known in the art to insert a plurality of restriction enzyme sites into linker regions so as to permit the correct orientation of the inserted sequence. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ a linker containing a Sal I site in order to facilitate the correct insertion of a sequence of interest which itself contained one or more Sal I sites.

Claims 74 and 75 are rejected under 35 U.S.C. § 103 as being unpatentable over the combined teachings of Gorman (US 5,024,939) and van Zonneveld et al. (1986).

Claim 74 adds a signal sequence to the expression vector of claim 61 and claim 75 contains the further limitation that the signal sequence employed be that of human tissue plasminogen activator.

Gorman (US 5,024,939) has been discussed above.

van Zonneveld et al. discloses expression vectors for the expression of human tissue-type plasminogen activator and in particular demonstrates that the signal sequence is effective even with truncated coding sequences suggesting that it functions independently of, autonomously of, the downstream coding sequences. Applicants also state at page 48 of the instant specification

In order to achieve optimal secretion of gp 160 from mammalian tissue culture cells, the 5' end of the coding sequence was modified to accept a heterologous signal sequence known to direct efficient secretion of both the homologous gene (human tissue plasminogen activator) and deletion variants of this gene. van Zonneveld et al. (1986) Proc. Natl. Acad. Sci. USA 83:4670.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include a signal sequence to facilitate the secretion or membrane association of a polypeptide of interest, particularly

wherein only a portion of the polypeptide of interest is being expressed, and more specifically to utilize the signal sequence element taught by van Zonnefeld et al. as it is taught to function autonomously of the coding sequences downstream from it.

5 Alternatively, it would have been obvious to insert the hTPA signal and coding sequences taught by van Zonnefeld et al. into the vector of Gorman (US 5,024,939) in order to achieve greater expression of the hTPA gene.

10 The vector construct of Example 2.3.2 is novel and unobvious and would be allowable if properly claimed. In view of the teachings of Gorman with regard to the effects of introns on expression the scope of allowable subject matter is unclear. It is anticipated that applicant will present **factual** argument in support of claims broader in scope than the vector of Example 2.3.2.

15 Claim 71 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

20 Any inquiry concerning this communication or earlier communications from the examiner should be directed to MP Woodward whose telephone number is (703) 308-3890. The examiner can normally be reached on Monday-Thursday and alternate Fridays from 8:30 AM to 5:30 PM.

25 If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christine M. Nucker, can be reached on (703) 308-4028.


Serial No. 08/288336
Art Unit 1813

-10

The fax phone number for this Art Unit is (703) 305-7939.

Any inquiry of a general nature or relating to the status of this application
or proceeding should be directed to the Group receptionist whose telephone
5 number is (703) 308-0196.

10


MICHAEL P. WOODWARD
PRIMARY EXAMINER
GROUP 1800

April 24, 1996